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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,328	12/09/2004	Jeffrey A Smith	00789-05	7405

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UNIVERSITY OF VIRGINIA PATENT FOUNDATION
250 WEST MAIN STREET, SUITE 300
CHARLOTTESVILLE, VA 22902

EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/517,328	SMITH ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *10-20 and 39-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 21-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election of Group V, claims 21-32, with traverse, in the response filed 10/31/2005 is acknowledged. The traversal is on the grounds that Group V utilizes a compound of general structure III for treating a disorder or disease characterized by inappropriate Rsk activity while Group III also utilizes compound of structure III for inhibiting Rsk activity. Hence Groups V and III have the same general technical feature regarding compound III and regulation of Rsk activity. Group I is drawn to a pharmaceutical composition comprising compound I, of which compound III is a species. Hence Groups V, III and I have unity and should be joined and examined on the merits. This argument is not found to be persuasive. The special technical feature of Group V is a method of treating a disease or a condition characterized by inappropriate activity, which is not the same as Groups III, which is drawn to inhibiting Rsk activity. Inhibiting Rsk activity doesn't necessarily mean that any disease or condition characterized by inappropriate Rsk activity can be treated. The Examiner has decided to rejoin Group I, claims 1-9 and 33-38 with elected Group V, claims 21-32 for examination.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-20 and 39-46 have been withdrawn from consideration as being drawn to non-elected subject matter. An action on the merits of Group I, claims 1-9 and 33-38 and Group V, claims 21-32 is contained herein below.

Specification

The disclosure is objected to because of the following informalities: Applicants have file the first page of the WIPO document for the abstract, which is not acceptable. An abstract typed on a separate sheet should be filed. Appropriate correction is required.

Priority

Applicants claim to priority under 35 USC 119(e) to US Provisional Application Serial No. 60/388,006filed June 12, 2002 and 60/449,553 filed February 24, 2003 is acknowledged.

Claim Objections

In claim 29 a comma should be inserted between the terms "hydroxyl" and "-$OCOR_4$".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of some particular and specific neoplastic tumors or cancers, does not reasonably provide enablement for the treatment of any other disease or conditions characterized by inappropriate activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art

(C) The level of one of ordinary skill
(D) The level of predictability in the art
(E) The amount of direction provided by the inventor
(F) The existence of working examples
(G) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claim 21 is drawn to a method of treatment of a disease or a condition characterized by inappropriate Rsk activity comprising the step of administering to a human or a mammal in need thereof a composition comprising a compound represented by general structure III. The breadth of the claim is seen to include some diseases including ones not yet discovered.

The state of the prior art

The examiner notes that Bjorbaek et al (WO 00/66721) discloses treatment of weight gain, obesity, reducing fat, leptin levels and increasing oxygen consumption by regulating the activity of Rsk.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the instantly claimed method may have a reasonable expectation of success. There is not seen sufficient data to substantiate that any disease or condition characterized by inappropriate Rsk activity can be treated by administration of the active agent/composition as instantly claimed. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F .2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the

statute. In the instant case, the instant claimed invention is highly unpredictable since one of ordinary skill in the art cannot fully describe the genus based on a few species.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the treatment of any disease or condition characterized by inappropriate Rsk activity. The specification also fails to direct the skilled artisan in correlative prior art procedures which might provide the basis for such a treatment.

The existence of working examples

The working examples set forth in the instant specification are drawn to inhibition of proliferation of cells. Despite this example there is no enabling disclosure for the treatment of any other diseases and conditions using the active agents as instantly claimed. One of ordinary skill in the art would not extrapolate the treatment efficacy of the active agents as instantly claimed for the treatment of any disease or condition characterized by inappropriate Rsk activity.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the treatment of any disease or condition characterized by inappropriate Rsk activity using the compound and composition as instantly claimed. The specification fails to provide clear and convincing evidence in sufficient support of the broad use of any compounds having those functions recited in the instant claims, as a result, necessitating one of ordinary skill in the art to perform an exhaustive search and undue experimentation for the embodiments of

any known and unknown compounds having those functions encompassed in the instant claims suitable to practice the claimed invention. One of ordinary skill I the art would also have to engage in undue experimentation to test all compounds encompassed by the instant claims and their combinations employed in the claimed compositions to be administered to a host, with no assurance of success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 25 recite the terms, " inappropriate Rsk activity". Even though the specification, at page 28, recites what inappropriate activity may be, it is still not clear what applicants intend by inappropriate activity. In the absence of a recitation of the specific activity the claims are rendered indefinite. For the purpose of prosecution the claims are examined as drawn to any disease or condition wherein Rsk activity is involved.

Claims that depend from rejected base claims that are unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Matthes et al (Phytochemistry, 1980, 19, 2643-2650).

Matthes et al disclose a compound of structural formula 7, wherein two of the three hydroxyl groups on the sugar moiety are acetylated (page 2645). This compound is structurally same as the compound claimed in instant claims 1 and 4-9. Matthes discloses that it has an extinction coefficient of c= 0.13 in ethanol (EtOH; page 2647, lines 22-24). This means that the extinction coefficient was measured as a solution in ethanol. The ethanol solution of the compound of formula 7 of Matthes is a pharmaceutical composition (limitation of claim 1).

This teaching of Matthes et al is seen to meet the limitations of instant claims 1 and 4-9.

Claims 25-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Bjorbaek et al (WO 00/66721).

Bjoebaek et al teach a method of modulating body weight, fat content, leptin levels or oxygen consumption by altering or modulating Rsk activity using nucleic acid construct expressing Rsk2 or a biologically active fragment thereof (page 2, lines 1-13; page 21, lines 1-7; example at pages 24 through 31; treatment of disease/condition characterized by inappropriate Rsk activity). The compounds of their invention can be used in the form of compositions (page 23, line 8 through page 24, line 20).

This teaching of Bjorbaek et al is deemed to meet the limitations of instant claims 25-27.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-3 and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matthes et al (Phytochemistry, 1980, 19, 2643-2650) in combination with Bjorbaek et al (WO 00/66721), Marks et al (US 5,910,583) and Kuijpers et al (US 5,733,523).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Matthes et al disclose a compound of structural formula 7, wherein two of the three hydroxyl groups on the sugar moiety are acetylated (page 2645). This compound is structurally same as the compound claimed in instant claims 1 and 4-9. Matthes discloses that it has an extinction coefficient of c= 0.13 in ethanol (EtOH; page 2647, lines 22-24). This means that the extinction coefficient was measured as a solution in ethanol. The ethanol solution of the compound of formula 7 of Matthes is a pharmaceutical composition. Matthes teaches that the extract from the roots of Zingiber zerumbet was tested against a rat neoplastic liver cell strain and found to be cytotoxic (page 2643, left column, Introduction, second and third paragraph). Even though Matthes teaches a compound that shows cytotoxicity towards neoplastic cells and a composition, he does not teach a composition comprising compound 7 and an anti-tumor agent, an anti-sense oligonucleotide or an interfering nucleotide.

Bjoebaek et al teach a method of modulating body weight, fat content, leptin levels or oxygen consumption by altering or modulating Rsk activity using nucleic acid construct expressing Rsk2 or a biologically active fragment thereof (page 2, lines 1-13; page 21, lines 1-7; example at pages 24 through 31). The compounds of their invention can be used in the form of compositions (page 23, line 8 through page 24, line 20). However, Bjorbaek does not teach a composition comprising the nucleic acid constructs and an anti-tumor agent.

Kuijpers et al teach in general the use of antisense oligonucleotides and their pharmaceutical formulations for the treatment of tumors (see abstract, col. 1, lines 26-40) and Marks teaches in general a variety of uses for oligonucleotide formulations including treatment of tumors (col. 5, lines 9-25).

Based on the teachings of the prior art above it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising an Rsk specific inhibitor and an antitumor agent including extracts from Zingiber zerumbet as instantly claimed because pharmaceutical compositions comprising such active agents are individually taught in the prior art to have the same utility.

It would have been prima facie obvious to one of ordinary skill in the art to combine the teachings given above. The instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant claims, given the teaching of the prior art of a composition for use in the treatment of tumors, it would have been obvious to make a composition containing an Rsk specific inhibitor as taught by Bjorbaek and oligonucleotides and antisense oligonucleotides as instantly claimed, because the idea of doing so would have logically followed from their having been individually taught in the prior art.

Conclusion

Claims 1-9 and 21-38 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK

12/08/05

Shaojia A. Jiang
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